

**National Institute of Allergy and Infectious Diseases  
Division of Acquired Immunodeficiency Syndrome**

**Community Leadership Meeting**

**December 9, 20003**

**Clinical Center, Masur Auditorium  
NIH Campus, Bethesda, Maryland**

The NIAID Division of AIDS (DAIDS) held a meeting with community representatives in Masur Auditorium of the Clinical Center on the NIH Campus in Bethesda, Maryland on December 9, 2003. The purpose was to discuss the scientific research agenda, with a focus on reorganization and recompetition of the DAIDS trials networks.

DAIDS representatives included:

Dr. Edmund Tramont, Director, DAIDS  
Dr. Jonathan Kagan, Deputy Director, DAIDS  
Dr. Carl Dieffenbach, Director, Basic Sciences Program  
Dr. Margaret (Peggy) Johnston, Director, Vaccine and Prevention Research Program  
Dr. Sandra Lehrman, Director, Therapeutics Research Program  
Mr. Matthew Murguia, Director, Office of Program Operations and Scientific Operations  
Mr. Daniel C. Montoya, Senior Policy Advisor, Henry M. Jackson Foundation

Community representatives in attendance are listed on list attached at end of summary

**Opening Remarks**

Matthew Murguia welcomed the participants to the meeting. He said that this meeting was part of an ongoing effort to brief the community and solicit input and comments on the DAIDS scientific agenda and the future recompetition of all of the DAIDS clinical trial networks.

Dr. Edmund Tramont said the mission of DAIDS “to help end the HIV/AIDS epidemic through research.” He offered a quick review of the stages of the clinical trials process, concluding that the system would not work without volunteers.

Dr. Jonathan Kagan presented guiding principles for reviewing of the clinical trials networks. He described the networks as “the intellectual engines that drive the clinical research agenda.” The networks are investigator initiated, with broad input from colleagues and the community in shaping details of the protocols.

Dr. Kagan said that DAIDS is trying to better link and coordinate activity between the networks, both domestically and internationally. He believes that accountability at the grass roots level will help make the best use of resources, make decisions and assess priorities across the entire spectrum of HIV clinical research.

DAIDS envisions a new level of leadership that will include network chairs, DAIDS staff, and other outside members “to establish accountability for the networks and be responsible for allocating a portion of funds that the division spends.” This body will focus on unforeseen needs

and large trials that require significant resources. It will support both domestic and international sites.

Dr. Kagan differentiated between domestic sites that have existing infrastructure and need little support and international sites where significant capacity building must occur. DAIDS is developing a mechanism that would fund sites at the level necessary to maintain core facilities and capacity to allow those sites to participate in network research projects. He identified laboratory and data management functions as those that must be standardized and performed at consistently high levels across all of the sites.

He acknowledged the tension between the need for stability within network membership to carry out those protocols and the need to facilitate inclusion of ideas from non-network researchers.

## **Discussion**

Are the labs and data centers going to be separate entities?

*That has not yet been formalized, but the sense is that those operations are integral parts of the networks, and those bodies will “at least minimally express their preferences” with regard to lab and data center operations.*

What portion of clinical research is currently conducted outside of the networks?

*There are about 20 such clinical trials being conducted under R01 grants.*

How do you envision coordination of community participation in these activities?

*Community representatives should be meeting in parallel to network leadership.*

Can the community select their own representatives and leadership within this new structure or should the networks do that?

*The selection of community members for the new level of leadership would come from DAIDS, while each network will select its own leadership representatives.*

Community participation has worked well but that there probably is need for greater community involvement and coordination across the networks.

*The community should be empowered to seek greater opportunities to participate more broadly in this process.*

## **Coordinated Clinical Research – Overview by Dr. Peggy Johnston & Dr. Sandra Lehrman**

Dr. Johnston said that in developing a coordinated clinical research plan to end the epidemic, DAIDS set three goals:

- Stop new infections
  - Protect uninfected persons
  - Reduce infectiousness of infected persons

- Keep infected persons healthy
- Continue to pursue innovative translational research

Dr. Lehrman posed issues that need to be considered

- Applicability
  - What does it mean for the population as a whole and for specific sub-groups in particular
  - Trade-offs between research to answer scientific questions and research that is deliverable on a large scale
  - Trade-offs of quick and dirty versus slower and more focused activity that may answer questions in more detail
- Who gets randomized along the continuum of individual to community
- Where is the focus along the continuum of individual to family
- How are resources allocated between domestic and international agendas
- The use of long term clinical outcomes and surrogate markers

Dr. Johnston explained that a range of prevention tools is preferred because not all of them will prove to be completely effective all of the time. Those tools include vaccines, microbicides, therapies and vaccines to reduce viral load and hence transmission, behavior changes, and barrier methods. Research is further complicated by the as yet unresolved “clade issue” of whether a single vaccine will protect against infection from multiple clades of the virus or whether multiple and individualized vaccines and interventions will have to be developed that are customized to each clade.

She said that DAIDS expects to conduct 2-3 large phase III trials during the period 2006-2011 to evaluate vaccine candidates, not only for protection from infection, but also their impact on infection—whether it affects the viral set point—secondary transmission, and disease progression. She acknowledged that it will be challenging to select the best candidates to move into phase III trials.

The development of successful microbicides must confront issues of adherence in using the product during clinical trials, as well as the barrier effect of a placebo gel and the carrier of the microbicidal agent in evaluating the efficacy of those agents.

She stated the importance of behavioral change and the use of barrier methods such as condoms in ongoing prevention efforts.

Dr. Lehrman discussed the role of treatment in preventing new infections. The clearest example of this is short-term use of nevirapine to reduce mother to child transmission at the time of birth. Other interventions with a demonstrated impact in reducing transmission and new infections include treatment of coinfections, particularly those that result in genital ulcers that offer an easier route of entry. ARV that reduces viral load also appears to reduce sexual transmission of HIV.

She said “There is still a very important research agenda that remains” for keeping people healthy. Significant questions center around when to start therapy; when to switch regimens; what is the most effective way to stage regimens; and how to handle salvage therapy for those who have developed resistance to existing classes of ARVs. Other areas include immune preservation and restoration, better understanding the impact of natural and complementary products, and the development of diagnostics that are simpler to use and less expensive in diagnosing and monitoring disease, therapy, and side effects.

Drs. Johnston and Lehrman discussed issues of coordinating science that may be conducted by separate trials networks was also discussed. It has become increasingly important to integrate these activities through common definitions, standards, and data collection that allows for the integration and comparison of outcomes across trials. DAIDS increasingly views HIV as a family disease rather than one that just affects individuals.

## Discussion

How does DAIDS expect to coordinate things internationally when they haven't been able to do it domestically? Particularly when it looks like the investigators will be "the same usual suspects." This participant argued that whoever gets the data centers and labs are going to get funded.

*We have to be careful to keep what is good with the current system. We need to build a different culture among the network investigators and there is confidence they are beginning to get it.*

*In some ways the international situation is better because the silos aren't there. In developing countries researchers often do not have the luxury of specialization and are engaged in a wide variety of prevention and treatment activities. The downside is that often "the depth of expertise is not there."*

There is a need to advocate for the gay male population in Africa where cultural and social discrimination against that population is widespread, and to a lesser extent in the US. How does DAIDS plan to advance the research agenda for those at risk populations? How does NIH plan to integrate its research with that being done by other federal agencies such as CDC, SAMHSA, and in the areas of mental health?

*It is necessary to include the gay population in our trials because to get products that can be licensed requires we do trials in the United States. Those trials will have to include gay men and minorities.*

*DAIDS pointed out the PAVE (Partnership for AIDS Vaccine Evaluation) effort and Secretary Thompson's "One HHS" initiative involving NIH, CDC & DOD, as prodding better cooperation between agencies. The microbicides effort is one that cuts across a number of Institutes at NIH.*

Health care systems in Africa are transmitting HIV to people through the failure to exercise universal precautions. NIH needs to work on this issue. HIV is a family disease, not just within the context of Africa but also within the African American family.

*DAIDS needs the help of the community in thinking through how to build that trust with our own African American community to get their greater involvement in research. NIH is focused on research; the need for universal precautions is already established and implementation is the responsibility of programs such as those of the CDC and through the President's Emergency Plan for AIDS Relief (PEPFAR), where the first RFAs were recently released.*

How will the network agendas be integrated?

*Those details have not been worked out yet and DAIDS does not want to eliminate investigator initiated research, but it will be getting more directly involved with larger trials.*

Where does pharmacology fit into the research agenda? Do Africans and Asians metabolize drugs differently and do different clades of HIV responds differently to specific drugs? This participant asked how interpretable and transferable outcomes of trials in those countries would be to the US?

*DAIDS sees pharmacology as part of the research agenda. Nobody really “owns” those issues right now. The hope is that NIH could be a partner and catalyst in addressing this area, but sometimes when it pushes it generates resentment and opposition. DAIDS is working hard to make sure that databases are standardized to help answer these questions and he welcomed input in this area.*

The pediatric agenda really does have to be integrated across all of the boundaries of research, especially vaccines. How do you get therapeutics to implement programs to prevent MTCT when host governments oppose it?

*Many researchers working in pediatrics fear that focus will get lost if it is better integrated and they wish to maintain a separate program.*

*This questioner argued that infants clearly get infected during a six-month window following birth and this might be a particularly good population for studying the efficacy of a vaccine.*

There is a lack of integration of AIDS and oral health care. The participant spoke of a partner who had a KS lesion in his mouth that went undiagnosed because the doctor was embarrassed to ask him to take his denture plate out for a full examination.

This participant felt that there was not enough notice of this meeting. For more effective community participation, there has to be enough lead time to get permission from work to be here, and opportunity to eat and rest to be able to participate (especially for those with more advanced HIV disease), and get materials to people far enough in advance that they can read and think about them. He went on to say that “transparency is absolutely vital and necessary across the board...if you really want community input.” He felt that the community was once again an afterthought.

*DAIDS acknowledged that there are a lot of meetings taking place, and it was difficult pulling together the meeting on short notice. There will be additional meetings on the network recompetition and that further comments are encouraged via e-mail. The goal for this meeting was to provide an overview for the RFA process for the recompetition of the networks.*

*DAIDS admitted that there has been limited interaction with National Institute of Dental & Craniofacial Research and encouraged suggestions on further collaboration.*

HIV is a family issue and that can be overshadowed. This participant spoke of losing his wife and having two infected children. He was pleased to see that NIMH recently joined the PACTG and he was encouraged by talk of more inter-Institute collaboration.

How will the program create the infrastructure in developing countries that is necessary to conduct vaccine trials? And how will therapeutic drugs be paid for and be provided to those who become infected during vaccine trials?

*There is a need to increase capacity at trial sites in developing countries; DAIDS acknowledged that there are differing opinions on how great that capacity needs to be. Some of the products in development will fall out and never make it to phase III trials. Other partners will have to assist in building some of the necessary clinical infrastructure; DAIDS can't do it all.*

*Training is key, and it is part of the NIH mandate and plan. Communities respond best to people who look and act like them, and DAIDS is working to create this research capacity within the host partner nations.*

*DAIDS has domestic trials that they cannot fill in a timely manner, and that is one of the reasons why activities are being shifted overseas. DAIDS emphasized the need "to break the stovepipes down" to utilize core infrastructure across the fields of network research.*

*Legally, NIH can only engage in research, it cannot provide therapy for participants once a trial is completed. But at the same time, morally, one cannot leave those patients hanging. DAIDS is working to ensure that host governments will be better prepared to take on those responsibilities by the time those trials are completed.*

In an environment where funding is flat, "what is going to fall by the wayside" to pay for standardization of databases and other operations? The participant acknowledged that it made theoretical sense to turn the international sites into pluripotent ones, but she expressed concern that there is a small pool of investigators and care givers to draw upon in those nations.

She went on to say that domestic trials have not been able to enroll patients in some trials because they were "a day late and a dollar short." She wondered how that problem could be overcome in the more complex and challenging international environment. How does DAIDS integrate these programs in a timely manner? She thought it would take political will and catalyzing new leadership.

*The approach has to be multi-pronged, starting by making hard decisions both within DAIDS and within NIAID. It also will require bringing in other partners. Staff reminded the audience that NIAID controls only about half of the AIDS budget at NIH, and those resources will have to be engaged. Finally, host governments and NGOs such as the Gates Foundation will play their roles.*

*They are taking a variety of approaches to allow the international sites to associate with the networks that they need to associate with.*

*The failure of domestic trials to fully enroll patients "is because of insufficient accountability on the part of the networks to develop and carry out an agenda that meets the public health needs of the communities, and get that done in a time frame that makes sense. Frankly, that is not only an embarrassment but a colossal waste of money that undermines the confidence that the community has in the network leadership."*

*"We are trying to increase the accountability at the level of networks, and not simply the accountability that networks currently use within themselves at the level of their site. We*

*are trying to see the networks as part of a whole.” There was “a much greater collective will” for collaboration, in part because DAIDS has insisted upon it.*

*A partnership where DAIDS cannot dictate simply because it funds operations; rather common goals must be forged through a process of building consensus.*

A participant said that patient recruitment issues are related to the fact that the networks often are not open to private practice physicians, who treat a large portion of the patient population. As a result, they participate in industry trials and not those sponsored by DAIDS. He urged DAIDS to modify the structure of trials to include people who have the ability to enroll patients. Some funds and trial slots should be reserved for physicians who wish to participate at that level.

*DAIDS puts out RFPs and RFAs and people respond to them, and that is what they have to work with.*

*The participant said they had applied twice, unsuccessfully, to the CPCRA. He thought the rejection was because of weak scientific leadership. He added, “Be careful that you don’t structure a process that doesn’t allow people who are good at that piece not to be a part of the process. Because, you need patients as much as you need design ideas.”*

The concept of community is important. The epidemic continues to grow disproportionately among the Latino population and “good effort is no longer enough.” DAIDS must ensure that researchers are culturally competent to be able to work with this community and recruit and retain appropriate numbers of Latinos in clinical trials.

This participant urged them to think of the “security issue” of the epidemic growing south of the US border and the ease with which those individuals can come to the US. Often South American societies and governments discriminate against gays, who are the center of the epidemic in most of those countries. The US needs to work to change those attitudes. NIH needs to develop a strategic plan to deal with this region.

*Extended discussion focused in part upon differences between research and care. DAIDS enumerated efforts to enroll greater numbers of racial and ethnic minorities into trials that it supports. Yet, the participant maintained there was a need “to build a different house” in order to better serve Latinos.*

A participant described the longstanding relationships HOPE Worldwide has with patient communities throughout the world.

*Recent meetings are beginning to establish a dialog with the organizations such as HOPE Worldwide.*

Will the focus on building capacity at international sites affect the CFARS (Centers For AIDS Research)?

*The focus of the meeting today was on the networks, but that CFARs will continue to be supported.*

A participant acknowledged the great progress made with regard to therapies over the last decade. However, he saw the current approach for many as “drug-hopping.” There needs to be a more

strategic and long-term approach to developing new therapies for those who have run out of options.

Another participant spoke on the importance of getting greater input from the community, and “not just the cream of the crop,” and of insuring greater community participation at the highest levels of planning.

It was time for greater coordination and cooperation, and, if necessary, it should be forced. There is “a culture around the table” of those making network decisions that is based more on an old boy network than on who can deliver the patients to answer the research questions.

A participant said, “Announcements and RFPs don’t reach us” and if they did, we wouldn’t know how to write grant proposals. That is why they are working with industry. She suggested that DAIDS both simplify and open up the process.

Matthew Murguia noted some of the key words from the session: coordination, integration, standardization, accessibility, efficiency, accountability, and community. He thanked the participants and closed the meeting.

*National Institute Of Health*

**Division of AIDS (DAIDS)**

**Judith**

Vice P Community Leadership Meeting  
Americ “The Scientific Research Agenda”

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***Final Participants List***

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